

WHAT IS CLAIMED IS:

1. A sequestering subunit comprising an aversive agent and a blocking agent, wherein the blocking agent substantially prevents release of the aversive agent from the sequestering subunit in the gastrointestinal tract for a time period that is greater than about 24 hours.

2. The sequestering subunit of claim 1, wherein the blocking agent prevents release of at least about 90% of the aversive agent from the sequestering subunit.

3. The sequestering subunit of claim 2, wherein the blocking agent prevents release of at least about 95% of the aversive agent from the sequestering subunit.

4. The sequestering subunit of claim 3, wherein the blocking agent prevents release of at least about 99% of the aversive agent from the sequestering subunit.

5. The sequestering subunit of claim 1, wherein the time period is at least about 48 hours.

6. The sequestering subunit of claim 5, wherein the time period is at least about 72 hours.

7. The sequestering subunit of claim 1, wherein the blocking agent is a system comprising a first aversive agent-impermeable material and a core.

8. The sequestering subunit of claim 7, wherein the first aversive agent-impermeable material comprises a hydrophobic material.

9. The sequestering subunit of claim 7, wherein the first aversive agent-impermeable material comprises a polymer insoluble in the gastrointestinal tract.

10. The sequestering subunit of claim 9, wherein the polymer is a cellulose polymer or an acrylic polymer.

11. The sequestering subunit of claim 10, wherein the cellulose is selected from the group consisting of ethylcellulose, cellulose acetate, cellulose propionate, cellulose

acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose triacetate, and combinations thereof.

12. The sequestering subunit of claim 10, wherein the acrylic polymer is selected from the group consisting of a methacrylic polymer, acrylic acid and methacrylic acid copolymers, methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl methacrylate, poly(acrylic acid), poly(methacrylic acid), methacrylic acid alkylamide copolymer, poly(methyl methacrylate), polymethacrylate, poly(methyl methacrylate) copolymer, polyacrylamide, aminoalkyl methacrylate copolymer, poly(methacrylic acid anhydride), glycidyl methacrylate copolymers, and combinations thereof.

13. The sequestering subunit of claim 12, wherein the methacrylic polymer is an ammonio methacrylic copolymer.

14. The sequestering subunit of claim 7, wherein the aversive agent-impermeable material is selected from the group consisting of polylactic acid, polyglycolic acid, a co-polymer of polylactic acid and polyglycolic acid, and combinations thereof.

15. The sequestering subunit of claim 7, wherein the system further comprises a second aversive agent-impermeable material and wherein the core is coated with the first aversive agent-impermeable material, which, in turn, is coated with the aversive agent, which, in turn, is coated with the second aversive agent-impermeable material.

16. The sequestering subunit of claim 15, wherein the first aversive agent-impermeable material is the same as the second aversive agent-impermeable material.

17. The sequestering subunit of claim 7, wherein the aversive agent is incorporated into the core and the core is coated with the first aversive agent-impermeable material.

18. The sequestering subunit of claim 7, wherein the core comprises a water-insoluble material and the core is coated with the aversive agent, which, in turn, is coated with the first aversive agent-impermeable material.

19. The sequestering subunit of claim 18, wherein the water-insoluble material is selected from the group consisting of microcrystalline cellulose, a calcium salt, and a wax.

20. The sequestering subunit of claim 1, wherein the aversive agent is selected from the group consisting of an antagonist of a therapeutic agent, a bittering agent, a dye, a gelling agent, and an irritant.

21. The sequestering subunit of claim 20, wherein the therapeutic agent is an opioid agonist.

22. The sequestering subunit of claim 21, wherein the opioid agonist is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, cyclazocine, desomorphine, dextromoramide, dezocine, diamorphide, dihydrocodeine, dihydroetorphine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, etorphine, fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacylmorphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenazocine, phenomorphan, phenoperidine, piminodine, piritramide, proheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, derivatives or complexes thereof, pharmaceutically acceptable salts thereof, and combinations thereof.

23. The sequestering subunit of claim 20, 21 or 22, wherein the antagonist is selected from the group consisting of naltrexone, naloxone, nalmefene, cyclazocine, levallorphan, derivatives or complexes thereof, pharmaceutically acceptable salts thereof, and combinations thereof.

24. The sequestering subunit of claim 1, wherein the blocking agent is a tether to which the aversive agent is attached, thereby forming a tether-aversive agent complex, and the complex is coated with a tether-impermeable material, thereby substantially preventing release of the aversive agent from the subunit.

25. The sequestering subunit of claim 24, wherein the tether is an ion exchange resin bead.

26. A composition comprising a sequestering subunit of claim 1-15, 17, 18, 20 or 24-25 and a therapeutic agent in releasable form, wherein, optionally, the mechanical fragility of the sequestering subunit is the same as the mechanical fragility of the therapeutic agent in releasable form.

27. The composition of claim 26, which is an oral dosage form.

28. The composition of claim 26, wherein the sequestering subunit is coated with the therapeutic agent in releasable form, thereby forming a composite subunit comprising the sequestering subunit and the therapeutic agent.

29. The composition of claim 26, wherein the therapeutic agent in releasable form is in the form of a therapeutic agent subunit.

30. A capsule suitable for oral administration comprising a plurality of the composite subunits of claim 28.

31. A capsule suitable for oral administration comprising a plurality of sequestering subunits of claim 1-15, 17, 18, 20, 24, or 25 and a plurality of therapeutic subunits, each of which comprises a therapeutic agent in releasable form.

32. A tablet suitable for oral administration comprising a first layer comprising the sequestering subunit of claim 1-15, 17, 18, 20, 24, or 25 and a second layer comprising a therapeutic agent in releasable form, wherein the first layer is coated with the second layer.

33. The tablet of claim 32, wherein the first layer comprises a plurality of sequestering subunits.

34. The tablet of claim 32, wherein the therapeutic agent in releasable form is in the form of a therapeutic agent subunit and the second layer comprises a plurality of therapeutic subunits.

35. A tablet suitable for oral administration comprising a single layer comprising a therapeutic agent in releasable form and a plurality of the sequestering subunits of claim 1-15, 17, 18, 20, 24, or 25 dispersed throughout the layer.

36. The tablet of claim 35, wherein the therapeutic agent in releasable form is in the form of a therapeutic agent subunit and the tablet comprises an at least substantially homogeneous mixture of a plurality of sequestering subunits and a plurality of therapeutic agent subunits.

37. A method of preventing abuse of a therapeutic agent, which method comprises incorporating the therapeutic agent into the composition of claim 26.

38. A sequestering subunit comprising an aversive agent, a first aversive agent-impermeable material, a second aversive agent-impermeable material, and a core, wherein the core is coated with the first aversive agent-impermeable material, which, in turn, is coated with the aversive agent, which, in turn, is coated with the second aversive agent-impermeable material, wherein the first aversive agent-impermeable material and second aversive agent-impermeable material substantially prevent release of the aversive agent from the sequestering subunit in the gastrointestinal tract for a time period that is greater than 24 hours.